Ancient DNA and the origin of modern humans

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C
entral to the debate over the origin of modern Homo sapiens are arguments over the mode, location, and timing of the transition from large-brained “archaic humans” to anatomically modern human form. Some argue for an African replacement model, where modern Homo sapiens arose as a new species in Africa roughly 150–200 thousand years ago (ka), followed by their dispersal throughout the Old World replacing archaic human groups (including the Neandertals). Others argue for a multiregional interpretation, where the transition from archaic to modern humans took place within a single evolutionary lineage extending back as far as 2 million years ago (1, 2). Some variants of multiregional evolution suggest that the transition to modernity first occurred in Africa and was then shared across the Old World through gene flow, while others argue that modern traits appeared in different times and places, such that modern humans evolved through the coalescence of these changes (3). The basic difference between African replacement and multiregional evolution advocates is between those favoring speciation and replacement and those favoring evolution within a single species. The debate over modern human origins has been addressed using the fossil and archaeological records, as well as reconstructions of evolutionary history based on the examination of patterns of genetic diversity within and between populations of living humans. In 1997, the genetic evidence was extended to prehistoric samples with the successful extraction of a mitochondrial DNA (mtDNA) sequence from the European Neandertal specimen from Feldhofer Cave in Germany (4). Since then, Neandertal mtDNA has also been extracted from Neandertal specimens from Mezmaiskaya Cave in the northern Caucasus (5) and from Vindija Cave, Croatia (6). These studies noted the difference between the mtDNA of Neandertals and living humans, and they suggested that these differences reflect separate species status for the Neandertals, implying an African replacement, at least in Europe. An alternative interpretation is that Neandertals were a subspecies whose mtDNA became extinct but still contributed some ancestry. What has been lacking from this debate is a comparison of Neandertal and living human mtDNA with mtDNA from ancient fossils that are clearly anatomically modern. The article by Adcock et al. (7) in this issue of PNAS helps fill this void by providing data on the extraction of mtDNA sequences from Australopithecus fossil specimens dating between 0.2 and 62 ka, all of which are demonstrably anatomically modern. While these additional data do not resolve the debate, they do allow implications to be drawn regarding the evolutionary significance of mtDNA sequence differences between fossil and living humans.

Studies of the genetics of living humans focus on reconstructing our species’ history from the present-day patterns of genetic variation within and between populations (8, 9). The extraction of mtDNA sequences from fossils offers a new perspective for interpreting genetic variation and our species’ history. Instead of having to base all of our genetic analyses on a single point in time (the present), we have the potential to examine temporal as well as spatial genetic changes. The initial extraction of mtDNA from the Feldhofer Cave Neandertal (4) was rightfully hailed as a remarkable technical success, and also offered to many compelling evidence supporting the hypothesis that Neandertals were a separate hominid species (Homo neanderthalensis) that became extinct by 28 ka, rather than a subspecies (H. sapiens neanderthalensis) that contributed some genes to modern human ancestry. The distinctiveness of Neandertal mtDNA has been confirmed by analysis of sequences from the Mezmaiskaya Cave and Vindija Cave specimens (5, 6). The similarity of the three Neandertal specimens confirms that the first one was not a fluke and that Neandertal mtDNA is different. The question, however, is how different? Were Neandertals a separate species, as predicted by an African replacement model, or were they a separate subspecies, which can be accommodated under a multiregional model? How much of a genetic difference should we see under each model? It is clear that Neandertal mtDNA tends to lie outside of the range of sequence differences found among living humans. For example, Krings et al.’s (4) analysis of the hypervariable region I of the Feldhofer shows that the difference between Neandertal and living human mtDNA is more than three times that found among living humans. However, the average difference between the Feldhofer sequence and living humans is less than that found in two out of three comparisons of chimpanzee subspecies (10).

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Based on these comparative data, it could be argued that Neandertals, while different, were a separate subspecies, a position long argued by a number of anthropologists. Likewise, the fact that we find no mtDNA sequences in living humans as divergent as the Neandertals can be interpreted in several ways. This finding might be a reflection of species extinction, but it could also reflect the effect of genetic drift and lineage extinction. The observation that Neandertal mtDNA is no more similar to living European mtDNA than to other geographic regions has also been used to support replacement, but it could instead be explained by multiregional evolution, because continued gene flow between regional populations will lead to an equilibrium state where all living humans have the same degree of Neandertal ancestry, albeit perhaps at a low level (9).

To date, all of the work on very ancient mtDNA has been done on the Neandertals. Given the alternative interpretations cited above, it is clear that a broader comparative database is required to provide further resolution. The most pressing need has been ancient mtDNA sequences from anatomically modern fossils. Comparison of

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mtDNA of Neandertals with living humans involves comparing samples more than tens of thousands of years apart in age, raising an interesting and fundamental question—how much of the observed mtDNA difference is attributable to phylogenetic differences (if any) and how much is attributable to microevolutionary changes over time? How much difference should we expect in a mtDNA sequence from a very ancient fossil known to be anatomically modern?

Adcock et al.’s (7) paper provides some insight. They obtained ancient mtDNA sequences from 10 Australian fossil hominids, all agreed to be anatomically modern, rather than archaic, Homo sapiens. The Australian fossil record shows both morphologically gracile and robust individuals, variation that is usually interpreted as reflecting different sources of past immigration. The specimens analyzed by Adcock et al. (7) consist of four gracile specimens, three of which come from Holocene deposits less than 10 ka. The fourth specimen, Lake Mungo 3 (LM3), dates to roughly 60 ka. The other six specimens are morphologically robust and come from Kow Swamp, and date between 8 and 15 ka. The sampling of morphologically different specimens from different time periods provides valuable insight into modern human origins and the evolution of ancient DNA.

In terms of the modern human origins debate, the most significant finding is the divergence of the mtDNA for Lake Mungo 3, a fossil specimen that is older than at least two (and possibly three) of the Neandertal specimens and is also clearly anatomically modern. The LM3 sequence is the most divergent of all of the Australian fossils analyzed in their paper, providing an excellent example of a mtDNA lineage that existed in an ancient modern human but is absent in living humans (except for the insertion into chromosome 11 of the nuclear genome). Several studies have suggested that the deepest mtDNA branch in living humans is African (“Eve”), a point often used to argue for an African origin of modern humans and subsequent replacement (11), although this conclusion has been questioned (12). Adcock et al.’s (7) study shows clearly that when considering ancient mtDNA in addition to living mtDNA, the deepest branch is Australian. This result does not imply that modern humans originated in Australia, anymore than an African root demonstrates an African origin; the geographic root could exist in different times and different places depending on ancient population dynamics (12). Adcock et al. (7) clearly demonstrate the actual extinction of an ancient mtDNA lineage belonging to an anatomically modern human, because this lineage is not found in living Australians. Although the fossil evidence provides evidence of the continuity of modern humans over the past 60,000 years, the ancient mtDNA clearly does not, providing an excellent example of why the history of any particular locus or DNA sequence does not necessarily represent the history of a population. Adcock et al.’s (7) work does not reject an African replacement model, because the data do not provide evidence as to the actual origin of the first modern humans in Australia, but it does cast doubt on the conclusion that the absence of ancient mtDNA in living humans implies replacement. If the mtDNA present in a modern human (LM3) can become extinct, then perhaps something similar happened to the mtDNA of Neandertals. If so, then the absence of Neandertal mtDNA in living humans does not reject the possibility of some genetic continuity with modern humans.

Adcock et al. (7) also note that mtDNA sequence differences do not distinguish between recent gracile and recent robust Australian fossils, providing further evidence that population history is not necessarily the same for all loci or traits. Although anatomically modern, the morphologically robust specimens from Kow Swamp fall outside the range of skeletal metrics of living Australians, but they have similar mtDNA that cluster with living Australians with no clear differentiation of these groups. LM3, however, is more similar anatomically (gracile) to living humans, but it has a divergent mtDNA sequence. The key difference here is age—LM3 is the oldest specimen. The mtDNA of the more recent Australian fossils (0.2 to 15 ka) tend to cluster together, while the LM3 sequence, from 62 ka, is the most divergent. To me, this finding suggests the loss of a mitochondrial lineage over time attributable to drift, although natural selection (a “selective sweep”) is also a possibility. Studies of living human mtDNA can be useful in addressing recent evolution, but ancient mtDNA is needed to extend our interpretations further into the past. Lineage extinction implies narrower time depth for our reconstructions based only on living human mtDNA.

Mitochondrial (and nuclear) DNA analysis offers powerful tools for understanding the past, but the interpretations vary depending on the units of analysis. Comparative analysis of DNA from different species (e.g., chimpanzees and humans) allows us to make inferences regarding the timing of speciation (13). Analysis of DNA sequences from individuals within a single species (e.g., living humans) can allow us insight into ancient population dynamics, such as population expansions or migrations (14).

When analyzing mtDNA sequences from ancient fossils, such as Neandertals, it is not clear which interpretive model should be used—separate species or variation within an evolving lineage? The choice of model influences the interpretive meaning. If Neandertals were a separate species, then the mtDNA evidence can inform us about when this line split off from the ancestors of modern humans. If Neandertals are not a separate species, then these divergence dates mean little, and provide instead information on ancient patterns of population size and gene flow. Adcock et al.’s (7) study, with its clear demonstration of lineage extinction in modern humans, suggests that the conclusion of separate species status for Neandertals, while possible, is not conclusive.

The modern human origins debate can be informed by genetic data, both living and ancient, but can only be resolved by also considering the fossil and archaeological evidence. The picture presented by Adcock et al. (7) suggests that modern human origins were more complicated than once envisioned.